DOI: 10.20514/2226-6704-2019-9-4-280-289 UDC УДК 616.12-008.331.1-06:61624.-008.444-08

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BLOOD PRESSURE AND ARTERIAL STIFFNESS CHANGES DEPENDING ON THE DURATION OF CPAP NIGHT SESSIONS IN PATIENTS WITH SEVERE OBSTRUCTIVE SLEEP APNEA

Abstract

Numerous studies on the pathophysiological mechanisms of obstructive sleep apnea discover the relationship between obstructive sleep apnea and cardiovascular diseases, its contribution to the development of resistant hypertension and endothelial remodeling. Continuous Positive Airway Pressure (CPAP) is the only reasonable pathogenetic therapy in these patients. This treatment regimen implies the creation of a "pneumatic stent" with a given level of positive pressure on the inhalation and exhalation of the patient, allowing to stabilize the lumen of the upper respiratory tract and prevent the pharyngeal collapse. However, the effects and the required duration of CPAP night sessions to achieve the target values of blood pressure and restore arterial stiffness in patients with severe obstructive sleep apnea with resistant hypertension remain poorly understood. **Objective:** To study the dynamics of blood pressure, arterial stiffness and endothelial dysfunction in patients with severe obstructive sleep apnea with resistant hypertension, depending on the duration of auto-adjusting CPAP (A-Flex mode). **Methods:** The prospective single-center study enrolled 168 patients aged 35–75 y. o. with obstructive sleep apnea and resistant hypertension (139 males (82.7 %) and 29 females (17.3 %), 46.4 ± 9.0 y. o.) with apnea-hypopnea index >30 events/hour. The patients signed the informed consent and obtained adjusted antihypertensive treatment. The night polygraphy study was performed to calculate AHI, oxygen desaturation index, mean nocturnal saturation (SpO_2) according to the requirements of American Academy of Sleep Medicine. Endothelial function of blood vessels was assessed manually according to peripheral arterial tone. The reactive hyperemia index and augmentation index was calculated. Blood pressure was monitored by office measurement, daily monitoring of blood pressure, and by individual patient diaries. Optimal level of CPAP-treatment was adjusted on an outpatient basis. Apnea-hypopnea index, the level of air leakage, average pressure and compliance to CPAP-therapy were established in accordance with the international requirements. **Results:** In the group of patients, treated with night sessions of A-Flex >6 h/night, significant dynamics was observed by the 6th month of treatment. That is, a decrease in RHI by –1.33 (95 % CI [–2.25; –0.41]; P = 0.002), a decrease in AI by –12.4 % (95 % CI [–18.42; –6.38]; P = 0.001), a decrease in mean SBP (24 h) by –33.6 mm Hg (95 % CI [–44.1; –23.2]; P = 0.002) and decrease in mean DBP (24 h) by –20.2 mm Hg (95 % CI [–29.4; –11.1]; P = 0.001), with a decrease in SBP RMR by –22.4 mm Hg/h (95 % CI [–24.7; –20.1]; P = 0.002), and a decrease in DBP RMR by –17.4 mm Hg/h (95 % CI [–19.5; –15.3]; P = 0.003). The best target values were achieved by the 12th month of treatment: a decrease in RHI by –2.11 (95 % CI [–2.57; –1.65]; P = 0.001), a decrease in AI by -28.5 % (95 % CI [–37.06; –19.94]; P = 0.002), a decrease in mean SBP (24 h) by –39.7 mm Hg (95 % CI [–48.9; –30.5]; P = 0.001) and decrease in mean DBP (24 h) by –26.8 mm Hg (95 % CI [–36.1; –17.5]; P = 0.001), with a decrease in SBP RMR by –22.5 mm Hg/h (95 % CI [–23.6; –21.4]; P = 0.001), and a decrease DBP RMR by –19.4 mm Hg/h (95 % CI [–20.7;

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–18.1]; P = 0.002). **Conclusions:** In patients with severe obstructive sleep apnea and resistant hypertension only CPAP-therapy in the A-Flex mode >6 h/night allows to achieve target blood pressure, restores endothelial function and arterial stiffness, therefore reducing the risk of cardiovascular complications.

Key words: *obstructive sleep apnea, resistant hypertension, arterial stiffness, endothelial dysfunction, CPAP-therapy, A-Flex mode*

Conflict of interests

The authors declare no conflict of interests.

Source of financing

The authors state that no finding for the study has been received.

Article received on 05.05.2019

Accepted for publication on 08.07.2019

For citation: Gorbunova M. V., Babak S. L., Adasheva T. V. et al. BLOOD PRESSURE AND ARTERIAL STIFFNESS CHANGES DEPENDING ON THE DURATION OF CPAP NIGHT SESSIONS IN PATIENTS WITH SEVERE OBSTRUCTIVE SLEEP APNEA. The Russian Archives of Internal Medicine. 2019; 9(4): 280-289. [In Russian]. DOI: 10.20514/2226-6704-2019-9-4-280-289

AHI — apnea-hypopnea index, AI — augmentation index, CPAP — Continuous Positive Airway Pressure, ODI — oxygen desaturation index, PAT signal — peripheral arterial tone, RH — reactive hyperemia, RHI — reactive hyperemia index, PWA — pulse wave amplitude, SpO_2 — level of blood saturation, BP — blood pressure, BPV — blood pressure variability, DBP — diastolic blood pressure, OSA — obstructive sleep apnea, PG — polygraphic study, ResH — resistant hypertension, SBP — systolic blood pressure, ABPM — ambulatory blood pressure monitoring, SNS — sympathetic nervous system, RMR — rate of morning rise, CRM — Center of Respiratory Medicine, HR — heart rate

Introduction

Obstructive sleep apnea (OSA) is associated with periodic development of upper respiratory tract collapses during nighttime. As a result of respiratory arrests, alveolar ventilation changes, and acute hypoxemia episodes with sharp increase in breathing efforts and substantial change in intrathoracic negative pressure occur. Large-scale prospective clinical studies proved the relationship between OSA and increased risk of cardiovascular diseases, including resistant hypertension (ResH) [1, 2]. Intermittent hypoxemia (cyclic desaturation with fast reoxygenation) occurring at the time of sleep apnea contributes to the formation of reactive oxygen intermediates, activates oxidative stress, and initiates endothelial vascular injury cascade [3]. Chronic inflammation results in vascular injury with further remodeling of blood vessels. Currently, arterial stiffness is recognized as a criterion of vascular ageing and a risk factor of cardiovascular events [4, 5]. Moreover, activated sympathetic nervous system (SNS), and amplified peripheral and central chemoreflexes cause a steady increase of blood pressure (BP) [6]. By removing pharyngeal collapses, Continuous Positive Airway Pressure (CPAP) therapy stops anoxemia episodes, reduces sympathetic tone and negative intrathoracic pressure fluctuations [7]. However, the duration of ventilatory care in patients with ResH+OSA is poorly understood, which was the reason for conducting this study.

Materials and methods

Study design

Our single-center prospective study enrolled 168 patients with hypertension and metabolic disorders (139 males, or 82.7 %, and 29 females, or 17.3 %), aged 46.4 ± 9.0 years, who had severe OSA (apnea-hypopnea index (AHI) >30 events/hour) and who had signed an informed consent (Figure 1).

All the patients underwent physical and complete medical examination with an additional focus on history, symptoms and markers of sleep respiratory disorders (STOP BANG Questionnaire) [8]. They were interviewed for how long they had been gaining weight and when it started, number of attempts to lose weight, administration of weight management medications and/or dietary supplements,

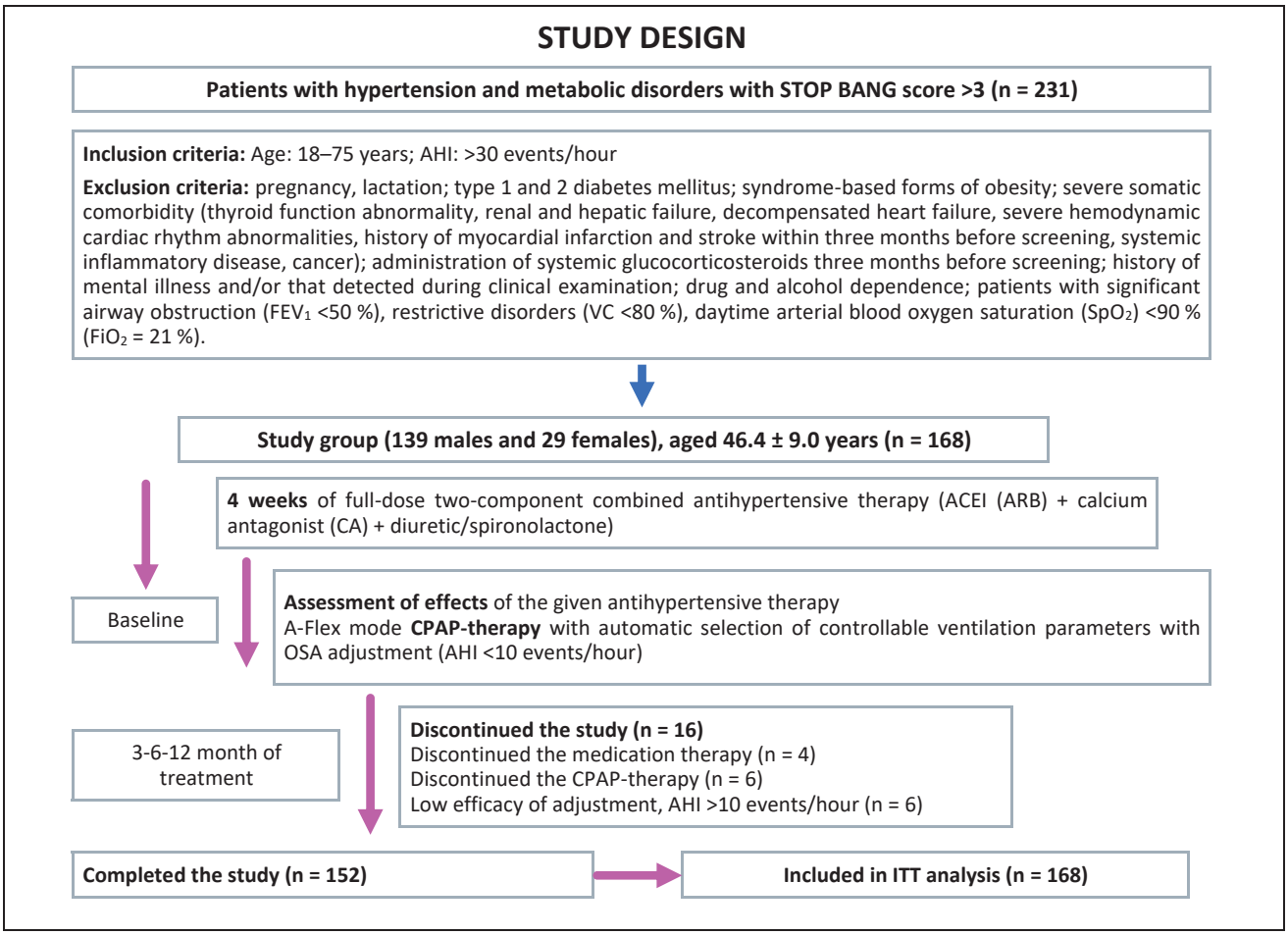

Figure 1. *Scheme of the study design. Explanations are given in the text*

dietary habits and daily dietary calories, physical activity. The exclusion criteria were: pregnancy, lactation; type 1 and 2 diabetes mellitus; syndrome-based forms of obesity; severe somatic comorbidity (thyroid function abnormality, renal and hepatic failure, decompensated heart failure, severe hemodynamic cardiac rhythm abnormalities, history of myocardial infarction and stroke within three months before screening, systemic inflammatory disease, cancer); administration of systemic glucocorticosteroids three months before screening; history of mental illness and/or that detected during clinical examination; drug and alcohol dependence; patients with significant airway obstruction (FEV_1 <50 %), restrictive disorders (VC <80 %), daytime arterial blood oxygen saturation (SpO_2) <90 % (FiO_2 = 21 %).

All patients received the full-dose two-component combination antihypertensive therapy (ACE inhibitors (ARB) + calcium antagonist (CA) + diuretic/spironolactone) [9] for 4 weeks with the assessment of effects of ResH medication adjustment in patients with OSA before respiratory support. In subsequent 3–6–12 months, all patients with OSA+ResH received auto-adjusting CPAP-therapy (A-Flex mode) in accordance with the recommendations of the American Academy of Sleep Medicine (AASM) [10] to achieve the optimal OSA adjustment with AHI <10 events/hour with preservation of the selected antihypertensive medication therapy.

Ethical standards

The study was conducted in the Department of Phthisiology and Pulmonology of the General Medicine Faculty at the A. I. Evdokimov Moscow State University of Medicine and Dentistry based

on the Center of Respiratory Medicine and the Hospital of Centrosoyuz of the Russian Federation (39 Losinoostrovskaya street, bldg. 2, Moscow, 107150, Russia). The study was approved by the Inter-University Ethics Committee of the A. I. Evdokimov Moscow State University of Medicine and Dentistry.

Polygraphic study

All the patients underwent a night polygraphic study (PG) as per the standardized protocol for cardiovascular monitoring of obstructive sleep apnea in accordance with the American Academy of Sleep Medicine (AASM) regulations and recommendations [11]. SOMNOcheck micro CARDIO (Lowenstein Medical (Weinmann), Germany) with SOMNOlab 2.19 (Lowenstein Medical (Weinmann), Germany) software was used. The study was started at 11.00 p. m. and completed at 7.30 a. m., with registration of the main polygraphic respiratory parameters: 1) mouth-nose airflow and snoring; 2) breathing efforts; 3) recording of SpO_2 and heart rate (HR) by pulse oxymetry. The polygraphy findings were processed manually by the qualified personnel of the CRM. Apnea was identified as reduction in the airflow signal by >80 % while maintaining the breathing effort for >10 seconds. Hypopnea was identified as reduction in the airflow signal by >30 % while maintaining the breathing effort for >10 seconds and subsequent desaturation by >4 %. Severity of OSA was determined by the apnea-hypopnea index (AHI) defined as the total number of obstructive apnea and hypopnea per 1 recording hour. Occurrence of 5< AHI <15 events/hour was assessed as mild OSA; 15< AHI <30 events/hour — as moderate OSA; AHI >30 events/hour — as severe OSA. The assessment included the nocturnal desaturation level by ODI, i. e., the number of drops of SpO_2 >4 %, as well as mean and minimum nocturnal saturation (SpO_2), respectively.

Endothelial function assessment

Vascular endothelial function was assessed by the quality of peripheral arterial tone (PAT signal) measured manually using two modified plethysmographic biosensors placed on forefingers of both hands [12]. Pulse wave amplitude (PWA) was estimated before and during reactive hyperemia (RH) by peripheral arterial tonometry (Endo-PAT2000, Itamar Medical Ltd., Israel). Ischemic stimulus was induced by cuff occlusion (shoulder cuff inflation up to systolic pressure of >200 mm Hg for 5 min), and the reactive hyperemia index (RHI) was calculated as a ratio of mean PWA for a period of 1 minute after cuff deflation to the baseline pre-occlusion PWA. We estimated the augmentation index (AI) defined as a ratio of the shock wave arising from the increase of aortic pressure to the systolic reflected wave [13]. All tests of RHI and AI were performed under standardized conditions (time, room, temperature).

Ambulatory blood pressure monitoring (ABPM) was performed using the BPLab 24-hour recording outpatient device, model MnSDP-2 (Petr Telegin, Russia). BP was recorded every 15 minutes during daytime and every 30 minutes at night. Sleep and wake intervals were determined individually, based on the patients' diaries. Examining 24-hour BP profile, we analyzed arithmetic means of systolic blood pressure (SBP), diastolic blood pressure (DBP) during day- and nighttime, as well as over 24 hours. To interpret the daily BP rhythm, the degree of nocturnal pressure reduction was used by calculating the daily index (DI, %) based on BP daily (BP_d) and nocturnal average values (BP_n), as calculated by the formula: $DI = 100\ \% \times (BP_d - BP_n)/BPd$. Based on the DI data, the following types of daily BP profile were determined: patients with normal nocturnal BP reduction (dippers): 10< DI <20 %; patients with insufficient nocturnal BP reduction (non-dippers): 0< DI <10 %; patients with higher nocturnal BP reduction (over-dippers): DI over 20 %; patients with steady increase in nocturnal BP (night-peakers): DI less than 0 %. Blood pressure variability (BPV) was assessed as a standard deviation of individual BP values from the daily and/or nocturnal mean value. Variability for SBP during day- and nighttime should not exceed 15 mm Hg, for DBP — 14 mm Hg during daytime and 12 mm Hg during nighttime. High BPV was registered when any of the four mentioned parameters deviated. The rate of morning BP rise was calculated by the ratio of the BP rise value to its time [14].

Assessment of compliance with CPAP-therapy

The optimum treatment level of CPAP-therapy was adjusted on an outpatient basis using pressure auto-select devices (PR System One REMstar Auto CPAP Machine with A-Flex (Philips Respironics, USA)) for 7 days following the diagnostic testing. To assess the compliance of patients with OSA on Month 3–6–12 of CPAP-therapy, we used Encore Pro v.2.14 original compliance analysis program (Philips Respironics, USA). The primary analyzed parameters included: 1) the mean time of CPAP-therapy for all days of usage (AU) (h/night) — an index that reflects the repeatability of CPAP-therapy in case of outpatient usage; 2) the average treatment pressure of CPAP-therapy (CMP) (mbar) — an index that reflects the treatment pressure of CPAP-therapy; 3) the average correctional apnea-hypopnea index during CPAP-therapy (AHI_{CPAP}) (events/hour) — an index that reflects the efficacy of CPAP-therapy. Based on the level of usage of nocturnal auto-adjusting CPAP-therapy (A-Flex mode), the patients were divided into the following groups: 1) <4 h/night — low compliant patients with OSA (group A); 2) 4 to 6 h/night — medium compliant patients with OSA (group B); 3) >6 h/night — high compliant patients with OSA (group C) [15].

Statistical analysis

Mathematical processing of the results was performed using the SPSS 12.0 software package (SPSS Inc., USA). Before the statistical analysis, the pattern of distribution of individual indicators was assessed according to the Kolmogorov — Smirnov test. The analysis was performed using single factor methods of parametric and non-parametric statistics. The Bonferroni method was applied for pairwise comparisons. If the quantitative attributes were distributed abnormally, the significance of group differences was examined using the Mann — Whitney U-test. Quantitative data was expressed as mean (M) and standard deviation (SD) (M±SD). During the final assessment of the findings, we performed the intention-to-treat analysis (ITT analysis) [16]. Moreover, methods of multivariate statistics should be used to reveal "hidden" factors affecting the result. The χ^2 test, the so-called likelihood ratio, was used to compare qualitative data; when no assumptions were made, the Fisher's exact test was applied. Differences in the tested parameters were considered significant at $p < 0.05$. When $0.05 < p < 0.1$, the existence of a statistical trend was estimated [17].

Results

Characteristics of the group with OSA+ResH (n = 168) after 4 weeks of the full-dose two-component combined antihypertensive therapy (ACE inhibitor (ARB) + calcium antagonist (CA) + diuretic/spironolactone) are presented in Table 1.

Of the 168 enrolled patients, a total of 152 (90.5 %) patients made every visit and were included in the standard analysis. Sixteen patients (9.5 %) discontinued their participation in the study by Month 12 due to: 1) self-determined termination of the medication therapy (n = 4); 2) self-determined termination of CPAP-therapy (n = 6); 3) low efficacy of A-Flex on Month 3 of observation with the preservation of AHI >10 events/hour (n = 6). All the patients were included in the subsequent ITT analysis.

It should be noted that, despite the full-dose combination medication therapy, patients with severe OSA+ResH had high BMI, severe nocturnal hypoxemia, and increased office SBP/DBP. They had low baseline RHI (endothelial function) and high baseline AI (arterial stiffness). The analysis of ABPM revealed a moderate increase in SBP/DBP with the expressed daily profile disturbance. The majority of patients (n = 115; 68.4 %) were assessed as non-dippers. They had increased blood pressure variability during day-/nighttime, as well as high rate of morning SBP/DBP rise.

Intention-to-treat (ITT) analysis of SBP/DBP, arterial stiffness and endothelial function

The mean medical pressure of CPAP-therapy (CMP) for all patients in the group was 14.40 ± 2.50 mbar with the apnea-hypopnea index (AHI_{CPAP}) adjusted to 6.90 ± 2.12 events/hour, which demonstrated that the OSA control target was achieved and the risk of probable fatal and non-fatal cardiovascular events was entirely eliminated [15].

Table 1. *Baseline characteristics of patients with hypertension+OSA (n = 168)*

Test parameter	BASELINE (n = 168)
Age (years)	46.40 ± 9.03
Gender (male/female)	139/29
Body mass index (BMI) (kg/m^2)	37.40 ± 3.60
Neck circumference (cm)	44.30 ± 3.81
Waist circumference (cm) males females	 121.40 ± 9.20 110.3 ± 11.60
Smokers (n, (%))	18 (10.7)
Ex-smokers (n, (%))	125 (74.4)
Never-smokers (n, (%))	25 (14.8)
Nocturnal polygraphic study (PG) parameters	
Apnea-hypopnea index (AHI) (events/hour)	49.8 ± 6.90
Oxygen desaturation index (ODI) (events/hour)	46.5 ± 4.70
Time required for saturation less than 90 % (TSat_90) (% of the total sleep time)	27.8 ± 3.40
Mean nocturnal saturation (Sat mean) (%)	83.1 ± 2.30
Minimum nocturnal saturation (Sat min) (%)	70.5 ± 4.20
Minimum nocturnal HR (beats/min)	43.1 ± 4.10
Maximum nocturnal HR (beats/min)	113.2 ± 7.30
Office SBP/DBP, reactive hyperemia index (RHI), augmentation index (AI)	
Hypertension duration, years	9.50 ± 2.90
Office SBP, mm Hg	163.20 ± 17.3
Office DBP, mm Hg	99.50 ± 7.11
Reactive hyperemia index (RHI) (reference <1.67)	3.30 ± 0.82
Augmentation index (AI) (%) (reference: 18.43–39.97 %)	47.10 ± 4.4
SBP/DBP ambulatory monitoring (ABPM) parameters	
Mean SBP (24 hours), mm Hg	151.1 ± 12.2
Mean DBP (24 hours), mm Hg	92.3 ± 10.1
Mean SBP (day), mm Hg	154.3 ± 13.4
Mean DBP (day), mm Hg	88.4 ± 8.3
Mean SBP (night), mm Hg	150.4 ± 12.1
Mean DBP (night), mm Hg	86.5 ± 7.4
SBP variability (day), mm Hg	22.4 ± 6.3
DBP variability (day), mm Hg	18.1 ± 2.4
SBP variability (night), mm Hg	25.3 ± 5.2
DBP variability (night), mm Hg	18.9 ± 4.6
dippers, (n, %)	7 (4.2)
non-dippers, (n, %)	115 (68.4)
night peakers, (n, %)	46 (27.4)
over-dippers, (n, %)	0 (0)
SBP RMR, mm Hg/h	29.6 ± 3.1
DBP RMR, mm Hg/h	23.4 ± 4.2

Table 2. *Changes in SBP/DBP, arterial stiffness and endothelial function parameters (n = 168)*

Test parameter	Baseline (without CPAP)	Month 3 CPAP	Month 6 CPAP	Month 12 CPAP
Reactive hyperemia index (RHI)	3.30 ± 0.82	3.10 ± 0.85	2.89 ± 0.92*	1.65 ± 0.46**
Augmentation index (AI) (%)	47.10 ± 4.4	45.20 ± 5.60	40.70 ± 6.02*	27.15 ± 8.56**
Mean SBP (24 hours), mm Hg	151.1 ± 12.2	133.2 ± 11.3*	124.2 ± 10.4**	119.4 ± 9.2**
Mean DBP (24 hours), mm Hg	92.3 ± 10.1	83.2 ± 10.1*	76.3 ± 9.2**	71.4 ± 9.3**
Mean SBP (day), mm Hg	154.3 ± 13.4	136.7 ± 11.4*	126.3 ± 10.3**	121.2 ± 9.5**
Mean DBP (day), mm Hg	88.4 ± 8.3	82.0 ± 8.1*	75.1 ± 7.3**	71.3 ± 7.3**
Mean SBP (night), mm Hg	150.4 ± 12.1	130.1 ± 11.7*	120.4 ± 9.1**	115.3 ± 9.2**
Mean DBP (night), mm Hg	86.5 ± 7.4	81.4 ± 7.2*	72.2 ± 6.1**	70.5 ± 5.4**
SBP variability (day), mm Hg	22.4 ± 6.3	15.4 ± 3.7*	11.3 ± 3.3**	10.5 ± 2.2**
DBP variability (day), mm Hg	18.1 ± 2.4	13.2 ± 2.5*	10.5 ± 3.4**	9.6 ± 2.8**
SBP variability (night), mm Hg	25.3 ± 5.2	15.7 ± 3.2*	10.5 ± 3.1**	10.1 ± 2.3**
DBP variability (night), mm Hg	18.9 ± 4.6	13.7 ± 3.9*	9.6 ± 2.3**	8.8 ± 3.1**
SBP RMR, mm Hg	29.6 ± 3.1	14.6 ± 3.9*	9.5 ± 2.3**	8.2 ± 1.1**
DBP RMR, mm Hg	23.4 ± 4.2	13.8 ± 2.7*	8.1 ± 2.1**	5.3 ± 1.3**

Note: RMR — rate of morning rise;
*ρ <0.05 against the baseline values (without CPAP), **ρ <0.01 against the baseline values (without CPAP)

We performed the intention-to-treat (ITT) analysis of SBP/DBP, RHI, AI adjusted for age, gender, BMI, conducted antihypertensive therapy, depending on the duration of daily night A-Flex sessions (CPAP-therapy). Changes in average values for the group (n = 168) of primary parameters on Months 3, 6, and 12 of the therapy are presented in Table 2.

In general, significant positive changes in SBP/DBP, RHI and AI against the background of CPAP-therapy occurred as early as Month 3. However, we found significant differences in the rate of achievement of the target test parameters depending on the duration of night sessions of A-Flex therapy. For example, patients who received A-Flex <4 h/night had the least changes (Figures 2, 3, 4).

Significant positive changes in the group of patients who received A-Flex >6 h/night occurred by Month 6: RHI decreased by –1.33 (95 % CI: –2.25 to –0.41; P = 0.002), AI decreased by –12.4 % (95 % CI: –18.42 to –6.38; P = 0.001), mean SBP (24-hour) decreased by –33.6 mm Hg (95 % CI: –44.1 to –23.2; P = 0.002) and mean DBP (24-hour) — by –20.2 mm Hg (95 % CI: –29.4 to –11.1; P = 0.001), with decrease of SBP RMR by –22.4 mm Hg/hour (95 % CI: –24.7 to –20.1; P = 0.002) and DBP RMR — by –17.4 mm Hg/hour (95 % CI: –19.5 to –15.3; P = 0.003). The best target values were achieved only in the group of patients who received A-Flex >6 h/night on Month 12 of A-Flex therapy: RHI decreased by –2.11 (95 % CI: –2.57 to –1.65; P = 0.001), AI decreased by –28.5 % (95 % CI: –37.06 to –19.94; P = 0.002), mean SBP (24-hour) decreased by –39.7 mm Hg (95 % CI: –48.9 to –30.5; P = 0.001) and mean DBP (24-hour) — by –26.8 mm Hg (95 % CI: –36.1 to –17.5; P = 0.001), with decrease of SBP RMR by –22.5 mm Hg/hour (95 % CI: –23.6 to –21.4; P = 0.001) and DBP RMR — by –19.4 mm Hg/hour (95 % CI: –20.7 to –18.1; P = 0.002).

Discussion

Obstructive sleep apnea is a heterogeneous disease with a complex development mechanism and high risks of cardiovascular complications [2]. In our study, we tried to analyze patients with hypertension and severe OSA who had the maximum risks of fatal events. Currently, CPAP-therapy is recognized

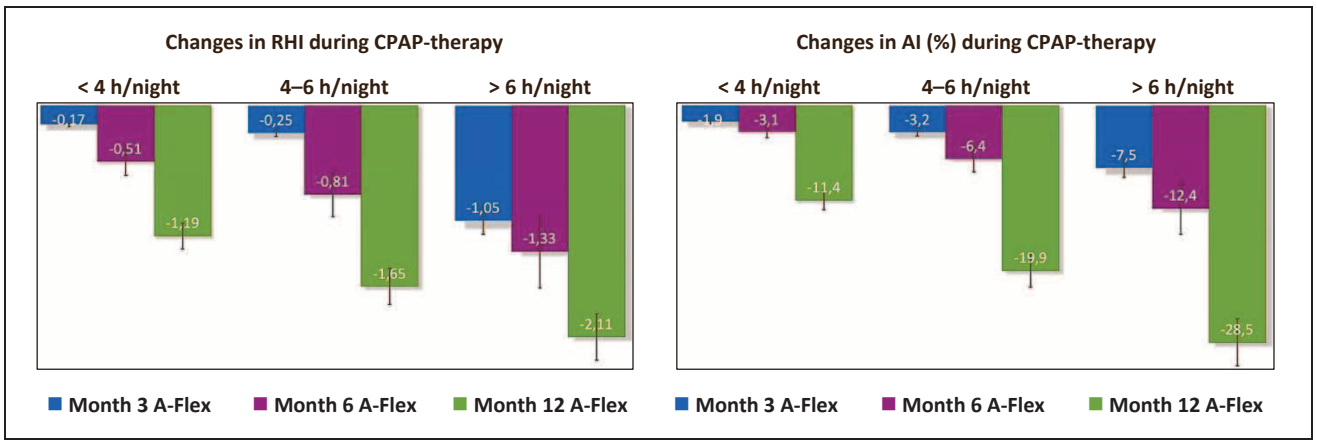

Figure 2. *Changes in RHI and AI depending on the duration of A-FLEX night sessions on Months 3–6–12. Explanations are given in the text*

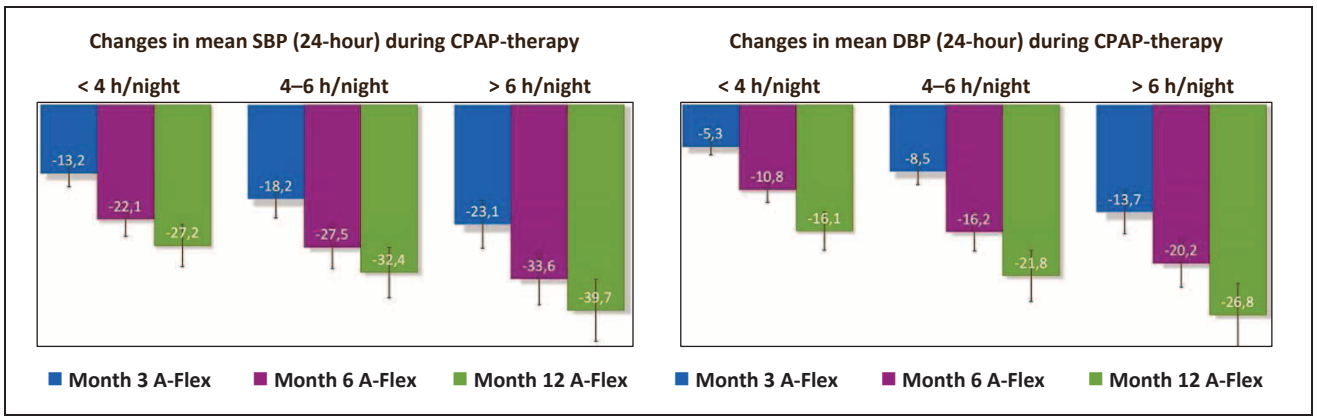

Figure 3. *Changes in mean SBP/DBP depending on the duration of A-FLEX night sessions on Months 3–6–12. Explanations are given in the text*

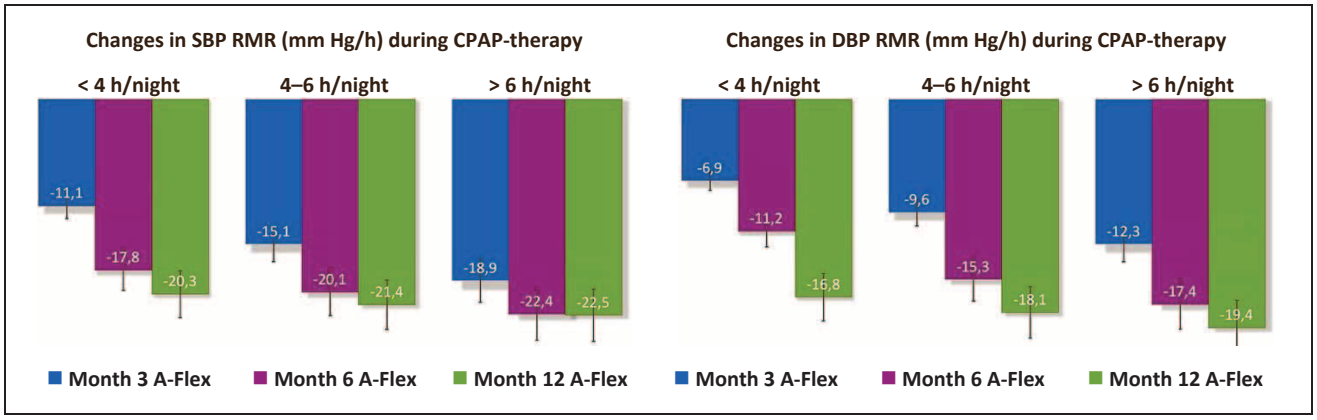

Figure 4. *Changes in rates of morning SBP/DBP rise depending on the duration of A-FLEX night sessions on Months 3–6–12. Explanations are given in the text*

as the only reasonable pathogenetic therapy for this disease [10]. However, various modes of CPAP and the required duration of night sessions are still understudied, especially for comorbid patients with OSA+ResH [18].

Despite the simple design, no blinding, placebo control and randomization of patients, we achieved the minimum effect on the endpoint through formation of the study group and use of the intention-to-treat (ITT) analysis [16].

Our findings are fully consistent with a number of studies on the impact of CPAP-therapy on the normalization of the endothelial function, arterial stiffness and blood pressure in patients with OSA [18, 19]. However, we first established special features of A-Flex night sessions in patients with severe OSA+ResH, when its duration of >6 h/night made it possible to achieve the target SBP/DBP, RHI and AI on Month 6. It should be noted that the low baseline efficacy of the full-dose combination antihypertensive therapy in patients with OSA is directly related to sleep fragmentation, nocturnal hypoxemia, nocturnal sympathetic activity [3]. This hypothesis is supported by our study when only combination full-dose drug and non-drug CPAP-therapy conducted for over 6 h/night significantly restores SBP/DBP, endothelial function and vascular stiffness to the target values, even in patients with severe OSA+ResH.

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